CASE REPORT

Gastropericardial Fistula and *Candida albicans* Pericarditis: A Rare Complication of Gastric Adenocarcinoma Treated with Radiation and Chemotherapy

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Gastropericardial fistula is generally associated with benign gastric diseases and is an uncommon complication of gastric adenocarcinoma. Pericarditis and cardiac tamponade are the ultimate outcome, with extremely high mortality rates. We report a 47-year-old man with gastric adenocarcinoma who had completed radiotherapy and was on scheduled chemotherapy, who presented with fever and chest pain. Gastric adenocarcinoma complicated with gastropericardial fistula and *Candida albicans* pericarditis were diagnosed and treated successfully with conservative management. Initial chest radiography and computed tomography (CT) revealed no evident pericardial air or fluid. However, follow-up panendoscopy 2 weeks later revealed a malignant ulcer with a fistula opening over the lesser curvature of the high body of the stomach. Subsequent chest radiography and CT revealed pneumopericardium with fluid accumulation. Emergent CT-guided pericardial drainage was performed. The fluid was positive for *Candida albicans*. Total parenteral nutrition and antifungal therapy were administered. The patient refused surgical intervention and survived with medical management alone. This case demonstrates that first, panendoscopy may be safely performed in patients with gastropericardial fistula without significant risk of cardiac tamponade; second, although early diagnosis of gastropericardial fistula is generally important, delayed recognition may not lead to devastating outcomes even in the absence of surgical intervention. [*J Chin Med Assoc* 2009;72(7):374–378]

Key Words: *Candida albicans*, gastric adenocarcinoma, gastropericardial fistula, pericarditis

Introduction

Pneumopericardium secondary to gastropericardial fistula is the accumulation of air or gas within the pericardial sac caused by a connection between the gastric cavity and pericardial space. It is a rare complication of laparoscopic surgery for reflux disease,[1,2] thoracic procedures, gastric ulcerations,[3–5] and positive pressure ventilation.[6] Without surgical intervention, the mortality rate is high. Fewer than 15 cases of pneumopericardium secondary to gastropericardial fistula as complications of peptic ulcer or malignancy have previously been reported.[7] Here, we report a patient with gastric adenocarcinoma undergoing radiotherapy and chemotherapy. Gastropericardial fistula and pneumopericardium were diagnosed by endoscopy. Notably, the patient survived with medical management alone.

Case Report

A 47-year-old man presenting with a 5-month history of gastric adenocarcinoma was admitted due to fever, chills and anterior chest pain. He had completed

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radiotherapy, with a total dose of 3,000 cGy in 15 fractions 2 months prior to this admission, and had been on chemotherapy for 5 months. The patient appeared febrile and weak, with a blood pressure of 128/73 mmHg, respiratory rate of 20/min, and pulse rate of 102/min. Heart sounds were normal, but the jugular vein was slightly engorged. Lungs, abdomen, and extremities were unremarkable.

On admission, the patient's white blood cell count, platelet count, and hemoglobin were 3,500/mm^3, 357,000/mm^3, and 8.6 g/dL, respectively. Serum level of alanine aminotransferase (ALT) was 12 U/L (normal, 0–40 U/L), of aspartate aminotransferase (AST) was 12 U/L (normal, 5–45 U/L), of total bilirubin was 0.7 mg/dL (normal, 0.2–1.6 mg/dL), of alkaline phosphatase was 104 U/L (normal, 30–70 U/L), of γ-glutamyl transpeptidase was 39 U/L (normal, 8–60 U/L), and of albumin was 3.5 g/dL (normal, 3.7–5.3 g/dL).

Chest radiograph revealed unremarkable findings (Figure 1A). However, chest computed tomography (CT) performed on the day following admission disclosed scanty pericardial effusion. Following hospitalization, a definite source of infection was not identified, and the patient experienced recurring fevers over the course of 2 weeks despite empiric antibiotic administration.

Two weeks following admission, upper gastrointestinal endoscopy was performed as part of a routine follow-up of the gastric adenocarcinoma. Endoscopy revealed a 3 cm ulcer with irregular margin over the lesser curvature of the high body of the stomach, and a fistula opening was found in the ulcer base (Figures 2B and 2C). Biopsy of the ulcer was done and pathologic evaluation confirmed its adenocarcinoma nature. Pneumopericardium was present on subsequent chest radiography (Figure 1B). Abdominal CT revealed retention of contrast medium in the stomach with

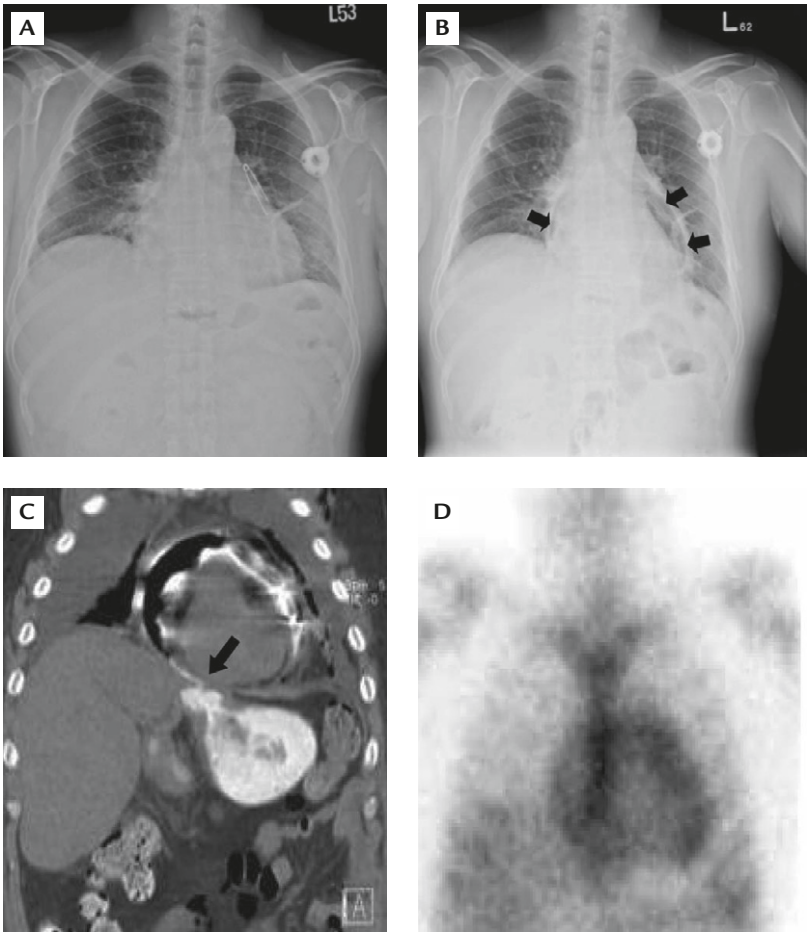

Figure 1. Chest radiography: (A) on admission; and (B) following panendoscopy, revealing pneumopericardium (arrows). (C) Abdominal computed tomography with coronal reformation shows radio-opaque contrast medium leaking from the stomach into the pericardial cavity (arrow). (D) Gallium scan exhibits a characteristic "halo" around the pericardial cavity.

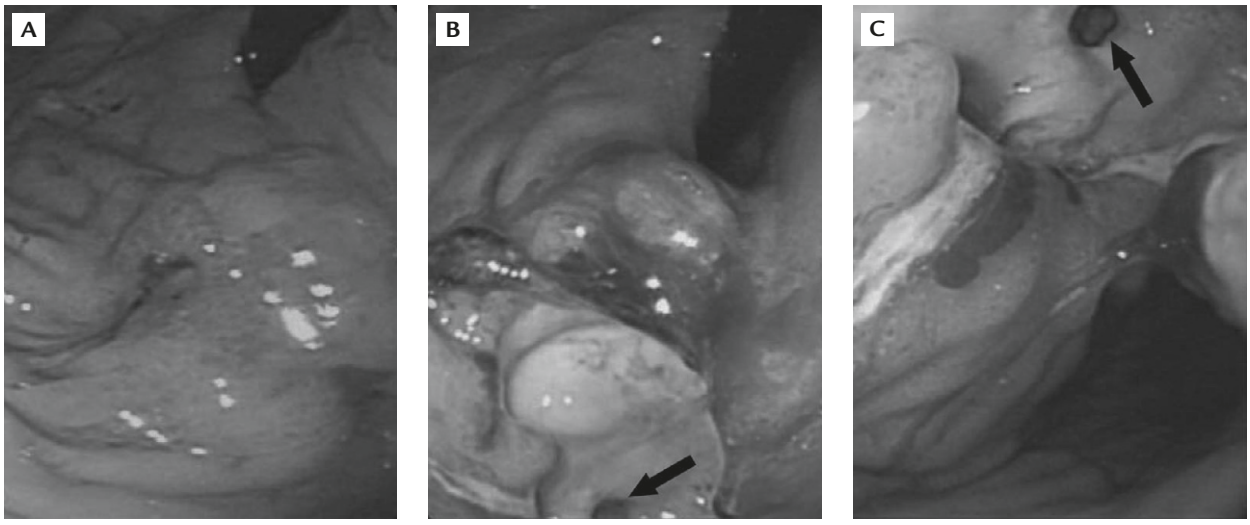

Figure 2. (A) Panendoscopy 6 months prior to admission demonstrates a gastric adenocarcinoma at the lesser curvature of the high body of the stomach. (B, C) Panendoscopy 2 weeks after admission reveals a large ulcer at the lesser curvature of the high body and a fistula opening at the base of the ulcerative gastric adenocarcinoma (arrow).

extravasation into the pericardial cavity (Figure 1C). Gallium scan showed a huge ovoid halo-shaped area with peripherally enhanced Ga-67 uptake around the heart (Figure 1D). There was no evidence of pneumothorax or pulmonary edema, and no pneumomediastinum was found. An emergent pericardium pigtail was placed under CT guidance. Ten milliliters of purulent fluid were drained, and the culture yielded *Candida albicans.*

Thoracotomy with fistula repair was suggested, but the patient refused surgical intervention. Total parenteral nutrition and intravenous fluconazole were therefore administered. Because of the stable hemodynamic status of the patient, he stayed in the ordinary ward during the course of conservative medical treatment. The pneumopericardium and fever resolved gradually 1 month after treatment. Abdominal CT with oral contrast was performed, and no contrast extravasation was found. The pigtail drainage tube was then removed successfully. At the 6-month follow-up, the patient did not complain of specific discomfort and tolerated further chemotherapy well. However, the patient was lost thereafter to follow-up.

Discussion

Gastropericardial fistula is an uncommon cause of pneumopericardium.[8,9] In a review of pneumopericardium caused by gastropericardial fistula, most identified cases were due to perforated gastric ulcers (6 of 7), and 1 was as a complication of radiation necrosis of gastric malignancy. [9] The risk of gastropericardial fistula caused by gastric ulcer increases with ulcers located in the cardia and fundus,[10–12] an ulcer in a hiatal hernia, or a history of hernia repair.[6,13,14] In addition, it has been reported that gastropericardial fistula can arise from malignant gastric ulcers[15,16] or in patients with radiation therapy for gastric malignancy.[17] Our patient is the first reported case of gastropericardial fistula resulting from malignant ulcer receiving both radiation and chemotherapy. The characteristics of the malignant ulcer *per se*, a chronic ulcer at the lesser curvature of the high body of the stomach treated with radiation and chemotherapy, may have predisposed our patient to development of a gastropericardial fistula.

Clinical symptoms and signs of gastropericardial fistula are variable, ranging from dysphagia, odynophagia, tachycardia, dyspnea, precordial tympany, and pericardial friction rub to severe chest pain. Acute onset of substernal pain is a common feature in these patients. Ultimate life-threatening cardiac tamponade presents in up to 37% of cases.[18] In our patient, chest tightness and dyspnea predominated at the beginning, which may have disguised early diagnosis. Ninety percent of pneumopericardium can be demonstrated by chest radiography, and the gastropericardial fistula tract can be visualized by contrast media studies in 70% of cases.[5] The typical appearance is a single transverse band of air on the frontal view of a chest radiograph.[19] For the gastropericardial fistula, contrast media-enhanced traditional examinations are the cornerstone of diagnosis. Abdominal CT may reveal the cause and connection between the fistulas. Our patient did not receive a conventional barium exam because residual barium may produce artifact on subsequent CT.

The rationale for panendoscopy in patients with gastropericardial fistula is controversial. Air insufflations may fill the fistula, causing pericardial tamponade with pulsus paradoxus and hemodynamic instability.[20,21] Indeed, hemodynamic changes were observed in experimental studies when 60 mL of air was injected into the pericardial sac.[8] The incidence of pericardial tamponade is even greater if *Candida* pericarditis is also complicated.[22] Yet, no case report has confirmed this potential complication induced by endoscopy. Nevertheless, only a few cases of gastropericardial fistula were diagnosed by endoscopy, including ours, with an en face view of the fistula (Figures 2B and 2C). Some authors recommend performing endoscopy in such cases in a controlled environment such as in the intensive care unit or operating room.[23] In our patient, chest radiography and CT revealed no evident pneumopericardium on the day of admission. It is quite possible that the endoscopy performed 2 weeks later made the pneumopericardium obvious in the following chest radiography. Fortunately, our patient did not have hemodynamic instability during or after endoscopy, which was performed in an ordinary endoscopic room without knowing about the presence of gastropericardial fistula beforehand. No cardiac tamponade occurred even though culture of the pericardial drainage demonstrated the presence of *C. albicans.*

The gastric mucosa is often an area of fungal colonization, with *Candida* infection detected in 54.2% of gastric ulcer cases and 10.3% of chronic gastritis cases.[24] Pericardial *Candida* infection often occurs in immunocompromised, antibiotic-treated, or postpericardiotomy patients.[22] In our patient, a malignant gastric ulcer with concurrent chemoradiation therapy and intensive antibiotic treatment during the hospitalization may account for the *C. albicans* infection in the pericardial fluid.

The mortality rate for gastropericardial fistula is reported to be as high as 85%.[18] Successful treatment includes early pericardial drainage, gastrostomy or corrective surgery,[25] with surgery being the definitive treatment.[7] Conservative medical treatment is mainly reserved for those with severe illness and carries a much higher mortality rate. Our patient is the third reported case of survival after conservative treatment with pericardiocentesis and antibiotics.[26,27]

In our case, the initial formation of gastropericardial fistula probably occurred at the time of admission. Pneumopericardium was detected by endoscopy 2 weeks later. This case is unusual in that the diagnosis was not early and the patient survived without surgical intervention. Our case emphasizes the importance of listing gastropericardial fistula as a differential diagnosis in a febrile patient experiencing chest pain and who has a history of gastric malignancy in the high body of the stomach and is undergoing concurrent chemoradiation therapy. Endoscopy is not contraindicated for diagnosis of gastropericardial fistula and carries a low risk of cardiac tamponade. Nevertheless, early diagnosis and surgical treatment of gastropericardial fistula remain crucial due to the high mortality rate with medical treatment alone.

References

1. Murthy S, Looney J, Jaklitsch MT. Gastropericardial fistula after laparoscopic surgery for reflux disease. *N Engl J Med* 2002;346:328–32.
2. Sihvo EI, Rasanen JV, Hynninen M, Rantanen TK, Salo JA. Gastropericardial fistula, purulent pericarditis, and cardiac tamponade after laparoscopic Nissen fundoplication. *Ann Thorac Surg* 2006;81:356–8.
3. Müller AM, Betz MJ, Kromeier J, Ghanem NA, Geibel A, Imdahl A, Frydrychowicz AP. Images in cardiovascular medicine. Acute pneumopericardium due to intestino-pericardial fistula. *Circulation* 2006;114:e7–9.
4. Simice P, Zwirewich CV. Gastropericardial fistula complicating benign gastric ulcer: case report. *Can Assoc Radiol J* 2000;51: 244–7.
5. Kaur H, Singh D, Kirschner ES, Maxwell JS. True heartburn: a case of gastropericardial fistula. *J Clin Gastroenterol* 2001; 32:458.
6. Schneider F, Schenk M, Tempe JD, Thiry L. Spontaneous gastropericardial fistula. *Ann Emerg Med* 1995;26:394.
7. Grandhi TM, Rawlings D, Morran CG. Gastropericardial fistula: a case report and review of literature. *Emerg Med J* 2004;21:644–5.
8. Cummings RG, Wesly RL, Adams DH, Lowe JE. Pneumopericardium resulting in cardiac tamponade. *Ann Thorac Surg* 1984;37:511–8.
9. Shackelford R. Hydropneumopericardium: report of a case with a summary of the literature. *JAMA* 1931;96:187–91.
10. Nicolaou N, Katz G, Conlan AA. Gastropericardial fistula presenting as acute cardiac tamponade: a case report. *S Afr Med J* 1984;65:51–2.
11. Ghahremani GG, Yaghmai S, Brooks JW, Hutton CF. Pneumopericardium due to transdiaphragmatic perforation of a gastric ulcer. *Am J Dig Dis* 1976;21:586–91.
12. Reisberg IR. Endoscopic antemortem diagnosis of gastropericardial fistula caused by perforation of benign gastric ulcer. *Gastrointest Endosc* 1974;21:27–9.
13. Edwards JR, Humeniuk V. Gastropericardial fistula. *Aust N Z J Surg* 1996;66:257–9.
14. Monro JL, Nicholls RJ, Hately W, Murray RS, Flavell G. Gastropericardial fistula: a complication of hiatus hernia. *Br J Surg* 1974;61:445–7.
15. Schein CJ, Judson GL, Hemphill AC. Gastropericardial fistula following transthoracic esophagectomy. *Ann Surg* 1949;130: 1074–8.
16. Harp VC, Peeke ES. Spontaneous pneumopericardium: case report. *Am Heart J* 1949;37:134–41.
17. Gottesman J, Bendick AJ. Pneumopericardium from radium necrosis. *Am J Med Sci* 1926;171:715–9.
18. Letoquart JP, Fasquel JL, L'Huillier JP, Babatasi G, Gruel Y, Lauvin R, Mambrini A. Gastropericardial fistula. Review of

the literature apropos of an original case. *J Chir* 1990;127: 6–12.
19. Van Gelderen WF. Stab wounds of the heart: two new signs of pneumopericardium. *Br J Radiol* 1993;66:794–6.
20. Wegryn RL, Zaroff LI, Weiner RS. Spontaneous tension pneumopericardium. *N Engl J Med* 1968;279:1440–1.
21. Berg RA. Pulsus paradoxus in the diagnosis and management of pneumopericardium in an infant. *Crit Care Med* 1990;18:340–1.
22. Rabinovici R, Szewczyk D, Ovadia P, Greenspan JR, Sivalingam JJ. *Candida* pericarditis: clinical profile and treatment. *Ann Thorac Surg* 1997;63:1200–4.
23. Cozart JC, Sundaresan S, Chokshi HR, Aliperti G, Walden DT. Gastropericardial fistula with pneumopericardium: an unusual complication of benign peptic ulceration. *Gastrointest Endosc* 1999;49:387–90.
24. Zwolinska-Wcislo M, Budak A, Bogdal J, Trojanowska D, Stachura J. Fungal colonization of gastric mucosa and its clinical relevance. *Med Sci Monit* 2001;7:982–8.
25. West AB, Nolan N, O'Briain DS. Benign peptic ulcers penetrating pericardium and heart: clinicopathological features and factors favoring survival. *Gastroenterology* 1988;94:1478–87.
26. Chapman PR, Boals JR. Pneumopericardium caused by giant gastric ulcer. *AJR Am J Roentgenol* 1998;171:1669–70.
27. Hall MN, Little JM. Penetration of the pericardium by a gastric ulcer: survival after pericardiocentesis. *J Am Board Fam Pract* 1990;3:289–91.